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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,049	05/22/2001	Sue J. Kenwrick	HO-P01961US1	8342

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/863,049	KENWRICK ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,32-39,43 and 51-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,32-39,43 and 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment and response filed on 9/2/03 has been entered. As requested, claims 6-8 and 50 have been canceled, and new claims 52-53 have been added. Claims 1-6, 32-39, 43, and 51-53 are pending and under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this office action, can be found in previous office actions. Please note that previous rejections/objections made on claims now canceled have been rendered moot by the cancellation of those claims.

Claim Rejections - 35 USC § 112

The rejection of pending claims 1-6, 32-39, 43, and 51-52 under 35 U.S.C. 112, first paragraph, for lack of scope of enablement, is maintained in modified form in view of applicant's amendments to the claims and arguments. Applicant's arguments as they pertain to the remaining grounds of rejection have been fully considered but have not been found persuasive in overcoming the following grounds of rejection.

The scope of enablement has been modified as follows: the specification, while being enabling for methods of detecting Incontinentia pigmenti (IP) in a human comprising the steps of

obtaining a sample from said human and analyzing said sample for an alteration in the nucleic acid sequence of the coding exons, introns, initiator codon, or stop codon of SEQ ID NO:1, wherein said alteration results in inactivation of NF-kB, does not reasonably provide enablement for methods of detecting IP in a human by analyzing a sample for an alteration in a regulatory nucleic acid, a promoter nucleic acid, the 5' untranslated region, or the 3' untranslated region of the nucleic acid sequence of SEQ ID NO:1, or for detecting an alteration in a nucleic acid of SEQ ID NO:1 in any organism. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The applicant argues that the claims have been amended to recite detecting IP in a human by analyzing the human NEMO sequence, specifically SEQ ID NO:1. However, while claims 1-5, and 51-53 are now limited to detecting alteration in SEQ ID NO:1 or human NEMO in a human, claims 32-39 continue to recite methods of detecting an alteration of SEQ ID NO:1 in any organism. The previous office action presented a detailed discussion concerning the lack of enablement for detecting alterations in SEQ ID NO:1 in organisms other than humans and further presented evidence that the NEMO gene is not responsible for IP in mice, and has not been linked to any disease or condition in any other organism. See pages 3-4 of the previous office actions, and also Aradhya et al. , Rudolph et al., and Baldwin et al. The applicant has not presented any arguments addressing these grounds of rejection, therefore the rejection of record over this aspect

of the invention for claims 32-39 is maintained. Please note that amendment of claims 32-39 to recite "a human" instead of "an organism" would overcome this grounds of rejection.

The applicant further argues that the specification provides an enabling disclosure for detecting mutations in non-coding regions of SEQ ID NO:1, including introns and the stop codon, citing page 7, lines 17-25, example 1 and example 3 in the specification. In view of applicant's arguments, the office has modified the scope of enablement to include mutations in SEQ ID NO:1 in humans in the introns, and the stop codon. However, the office maintains that the specification does not enable the full scope of the broadest claims which reads on mutations in regulatory sequences, promoter sequences, or the 5' or 3' untranslated sequences in SEQ ID NO:1 which correlate with IP in humans. SEQ ID NO:1, as noted by the applicants, is genomic DNA. While it is clear from the specification that SEQ ID NO:1 contains all the exons, introns, and at least the stop codon of the human NEMO gene, it is unclear whether SEQ ID NO:1 does in fact include the NEMO promoter and associated regulatory sequences. The specification provides no guidance for the sequence of the NEMO promoter, nor does it identify by structural features of specific sequences any "regulatory" sequences present in the NEMO genomic DNA as represented by SEQ ID NO:1. In addition, as discussed in detail in the previous office action, the specification fails to provide evidence linking mutations in the putative promoter or regulatory regions of SEQ ID NO:1 with inactivation of NF-kB and IP. Thus, while the applicants have provided substantial evidence linking deletions and mutations in the coding sequences, intron 3, and the stop codon of the human NEMO gene (SEQ ID NO:1) with Incontinentia pigmenti in

human patients with either the familial and sporadic versions of IP, the specification fails to identify or link any mutation with any regulatory, promoter, 3' or 5' untranslated sequence of the human NEMO gene. Furthermore, the applicant's references to Shahbazian and Zoghbi and Chaturvedi et al. do not supply the missing teachings. The Chaturvedi et al. and Shahbazian and Zoghbi references, both of which were published after the filing date of the instant application, teach mutations associated with Duchenne/Becker Muscular Dystrophy and Rett syndrome. Neither article teaches mutations in the human NEMO gene, or that mutations in the promoter or regulatory sequences of genes associated with Duchenne/Becker Muscular Dystrophy and Rett syndrome can be linked to either disease. The Chaturvedi et al. and Shahbazian and Zoghbi references, and the Mayer et al. and Bardaro et al. references listed in the supplemental IDS, all teach mutations in the codings exons or introns of genes which are responsible for disease phenotype. Therefore, in view of the lack of guidance provided by the specification for regulatory sequences or promoters associated with SEQ ID NO:1, the lack of guidance for mutations in the regulatory, promoter, or untranslated regions of SEQ ID NO:1 which are linked to IP in humans, the evidence of record which demonstrates that mutations which correlate with NF-kB inactivation are located in the coding exons, intron, or stop codon of SEQ ID NO:1, and the breadth of the claims, it would have required undue experimentation at the time of filing for the skilled artisan to identify mutations in the promoter, regulatory, or untranslated regions of SEQ ID NO:1 which correlate with IP in humans.

The rejection of pending claim 51 under 35 U.S.C. 112, first paragraph, for lack of written description for NEMO genes other than human NEMO, is withdrawn in view of applicant's amendment to claim 51 and arguments.

The applicant's amendments to the claims has resulted in the following new grounds of rejection of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, and 51-53 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of claim 1 and claim 51 have been amended to recite methods to detect Incontinentia pigmenti in a **human**. However, the method steps of claims 1 and 51 recite obtaining a sample from "said organism". There is no antecedent basis for "organism" in the claims as amended. Claims 2-5 and 52-53 depend on claim 1 and thus are included in this rejection. Please note that amendment of claims 1 and 51 to replace "said organism" with "said human" would overcome this grounds of rejection.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 872-9306.

Please note that the United States Patent and Trademark Office will begin to move to the new campus in Alexandria, Virginia, in December 2003. The examiners of Art Unit 1632 will be moving in January 2004. As of January 13, 2004, this examiner's phone number will be (571) 272-0737, and that of the examiner's supervisor will be (571) 272-0734.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER